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EXAMINER	
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Below is a communication from the EXAMINER in charge of this application

COMMISSIONER OF PATENTS AND TRADEMARKS

ADVISORY ACTION

☐ THE PERIOD FOR RESPONSE:

a) ☐ is extended to run _____ or continues to run _____ from the date of the final rejection

b) ☐ expires three months from the date of the final rejection or as of the mailing date of this Advisory Action, whichever is later. In no event however, will the statutory period for the response expire later than six months from the date of the final rejection.

Any extension of time must be obtained by filing a petition under 37 CFR 1.136(a), the proposed response and the appropriate fee. The date on which the response, the petition , and the fee have been filed is the date of the response and also the date for the purposes of determining the period of extension and the corresponding amount of the fee. Any extension fee pursuant to 37 CFR 1.17 will be calculated from the date of the originally set shortened statutory period for response or as set forth in b) above.

☒ Appellant's Brief is due in accordance with 37 CFR 1.192(a).

☒ Applicant's response to the final rejection, filed 1/20/2000 has been considered with the following effect, but it is not deemed to place the application in condition for allowance:

1. ☒ The proposed amendments to the claim and /or specification will not be entered and the final rejection stands because:

a. ☒ There is no convincing showing under 37 CFR 1.116(b) why the proposed amendment is necessary and was not earlier presented.

b. ☒ They raise new issues that would require further consideration and/or search. (See Note).

c. ☐ They raise the issue of new matter. (See Note).

d. ☒ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal.

e. ☐ They present additional claims without cancelling a corresponding number of finally rejected claims.

NOTE: See enclosed note

2. ☐ Newly proposed or amended claims _____ would be allowed if submitted in a separately filed amendment cancelling the non-allowable claims.

3. ☒ Upon the filing an appeal, the proposed amendment ☐ will be entered ☒ will not be entered and the status of the claims will be as follows:

Claims allowed: none
Claims objected to: n/a
Claims rejected: 1-30, 34-51, 53-56, 69, 70

However;

☐ Applicant's response has overcome the following rejection(s): _____

4. ☒ The affidavit, exhibit or request for reconsideration has been considered but does not overcome the rejection because the pending rejections as applied to the claims under consideration remain for the reasons of record. Also see enclosed note

5. ☐ The affidavit or exhibit will not be considered because applicant has not shown good and sufficent reasons why it was not earlier presented.

☐ The proposed drawing correction ☐ has ☐ has not been approved by the examiner.

☒ Other See enclosed note

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PRIMARY EXAMINER
GROUP 1800 1600

1. Proposed claims 34 and 35 raise new issues that would require further search and new potential rejections over the prior art. Said claims recite new limitations that were previously not recited in the claims.

2. Claims 1-13,53-56,69,70 stand provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-6 of copending application Serial No. 08/441259 . Although the conflicting claims are not identical because the scope of claim 1 of 08/441259 differs from that of the instant invention in that it recites that the cells are not lysed as part of the procedure, both sets of claims read on methods that encompass positive selection of cells secreting a particular protein. Therefore, the two sets of claims under consideration in this rejection would have been prima facie obvious in view of each other to one of ordinary skill in the art at the time the invention was made for the aforementioned reasons.

This is a *provisional* obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Applicant has indicated that a terminal disclaimer would be submitted at a later date if the instant application is found allowable.

3. Claims 1-21,29,30,34-40,43-50,53-56,69,70 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the claimed method or kit which uses a high viscosity or gel forming medium such as gelatin or agarose or alginate, does not reasonably provide enablement for the claimed method or kit that does not use said ingredients. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims for the reasons elaborated in the previous Office Action. Applicants arguments have been considered and deemed not persuasive.

Manz et al. teach that, "In normal medium the secreted product will readily diffuse away and, in the approach described here, will label all cells covered with the affinity matrix, whether they are secreting or not."(page 1923, first column). Manz et al. later point out that a solution to this problem is to perform the assay in a high viscosity media (page 1923, first column). Thus, Manz et al. establish the need for high viscosity media to practice the instant invention. Therefore, the enablement is not commensurate with the scope of claims that do not recite the aforementioned

ingredient as a component of the claimed method or kit.

Regarding applicants arguments, The MPEP section 2164.08 discloses:

> *2164.08 Enablement Commensurate in Scope With the Claims*
> *All questions of enablement are evaluated against the claimed subject matter. The focus of the examination inquiry is whether everything within the scope of the claim is enabled. Accordingly, the first analytical step requires that the examiner determine exactly what subject matter is encompassed by the claims. The examiner should determine what each claim recites and what the subject matter is when the claim is considered as a whole, not when its parts are analyzed individually. No claim should be overlooked. With respect to dependent claims, 35 U.S.C. 112, fourth paragraph, should be followed. This paragraph states that "a claim in a dependent form shall be construed to incorporate by reference all the limitations of the claim to which it refers" and requires the dependent claim to further limit the subject matter claimed.*
> *The Federal Circuit has repeatedly held that "the specification must teach those skilled in the art how to make and use the full scope of the claimed invention without `undue experimentation'." In re Wright, 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993).*

Manz et al. (an inventor of the instant application), discloses in a publication filed after the filing date of the instant invention, wherein said publication discloses the instant invention that, "In normal medium the secreted product will readily diffuse away and, in the approach described here, will label all cells covered with the affinity matrix, whether they are secreting or not."(page 1923, first column). Manz et al. later point out that a solution to this problem is to perform the assay in a high viscosity media (page 1923, first column). Thus, Manz et al. establish the need for high viscosity media to practice the instant invention. Regarding applicants comments, Manz et al. broadly characterize the method which they disclose (see Abstract) and state that: "Crossfeeding of the secreted products to other cells is prevented by decreasing the permeability of the incubation media." (see Abstract). This is accomplished using high viscosity media (page 1923, first column).

Therefore, the enablement provided in the specification is not commensurate with the scope of claims that do not recite the aforementioned limitation. Regarding Example 1 of the specification, said example actually discloses the need to use high viscosity media to actually distinguish secreting from nonsecreting cells (see page 28, last sentence, continued on next page). Example 1 in the specification indicates that depending on the parameters used, in the absence of high viscosity media it is not possible to distinguish secreting from nonsecreting cells (see page 27, last paragraph). Regarding the specification, page 18, Manz et al. teach that, "In normal medium the secreted product will readily diffuse away and, in the approach described here, will label all cells covered with the affinity matrix, whether they are secreting or not."(page 1923, first column). Manz et al. later point out that a solution to this problem is to perform the assay in a high viscosity media (page 1923, first column). Thus, Manz et al. establish the need for high viscosity media to practice the instant invention. Regarding the Assenmacher declaration filed 6/12/98, said declaration discloses that: "The requirement for embedding cells in media of high viscosity during the secretion period was overcome by optimizing incubation conditions with respect to cell density and incubation time."(page 3). Thus, the Assenmacher declaration filed 6/12/98 discloses that in order to obtain the results disclosed in said declaration it is necessary to optimize incubation conditions with respect to cell density and incubation time. However, the specification does not disclose such steps with regards to the claimed invention. Thus, the Assenmacher declaration filed 6/12/98 does not establish that the claimed invention is enabled in the absence of a high viscosity or gel forming medium such as gelatin or agarose or alginate because the Assenmacher declaration relies on a method which uses crucial steps wherein the crucial steps of the method are not disclosed in the specification.

In the phone interview with BPS Schwartz, SPE Chan and Examiner Schwadron that applicant refers to in page 2 of the instant amendment, this rejection was discussed and the conclusion was reached that said rejection would be addressed via submission of a declaration from an expert which would address the pertinent issues especially the issue of what did or did not constitute routine experimentation. No such declaration has been filed.

4. Claims 14,15,29,30 stand rejected under 35 U.S.C. § 102(b) as being clearly anticipated by Kohler et al. for the reasons elaborated in the previous Office Action. Applicants arguments

have been considered and deemed not persuasive.

Regarding applicants comments about proposed claim 14, said claim has not been entered. Regarding applicants comments, Kohler et al. teaches the methods of claims 14 and 15 (see page 469, section 2.8). Regarding applicants comments, Kohler et al. teach the method of claim 14, which is drawn to a method to label cells with a secreted product (see entire document), not a method to positively select cells. The cells are not lysed as part of the "labelling procedure" taught by Kohler et al.. The cells are not lysed until after the labelling procedure (eg. the cells are labelled with hapten, then in a separate step, the labelled cells are added to a source of complement, see section 2,8, page 469). Regarding applicants comments, claim 29 reads on progeny of cells which secrete a desired product (eg. hybridoma cells that secrete a desired antibody). The progeny of labelled cells produced by the claimed method will not be labelled because said cells are not the original labelled parent cells and the label or capture moiety would not be found on progeny cells. Therefore, the progeny of the cells of claim 29 are identical to hybridomas secreting a desired product (eg. any hybridoma cell). Kohler et al. teach hybridoma cells. Regarding cells separated by the claimed method, the labelled cells will not maintain the capture moiety/label for an indefinite period of time. All membrane bound molecules are eventually recycled and disappear from the cell surface after an appropriate length of time. After the capture moiety disappears from the cell surface, a hybridoma cell produced by the claimed method is identical any art hybridoma cell, such as those taught by Kohler et al. Regarding the process recited in claims 29 and 30, the method wherein the claimed product is made carries no patentable weight in said claims because the claimed product is identical to that of the prior art. The MPEP section 2113 (July 1998, page 2100-51) states:

Even though product-by process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985) (citations omitted) (Claim was directed to a novolac color developer. The process of making the developer was allowed. The difference between the inventive process and the prior art was the addition of metal oxide and carboxylic acid as separate ingredients instead of adding the more expensive pre-

reacted metal carboxylate. The product-by-process claim was rejected because the end product, in both the prior art and the allowed process, ends up containing metal carboxylate. The fact that the metal carboxylate is not directly added, but is instead produced in-situ does not change the end product.).

5. Claims 14-28,34-51 remain rejected under 35 U.S.C. § 103 as being unpatentable over Kohler et al in view of Hunt, Segal (US Patent 4,676,980) and prior art disclosed in the specification for the reasons elaborated in the previous Office Action. Applicants arguments have been considered and deemed not persuasive.

Regarding applicants comments in the instant amendment, proposed claims 14,34,35 have not been entered.

6. Claim 69 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for the reasons elaborated in the previous Office action. Applicants arguments have been considered and deemed not persuasive.

There is no support in the specification as originally filed for the methods of claims 69 and 70.

Regarding applicants comments there is no disclosure in the specification of the methods of claims 69 and 70. There is no written description in the specification as originally filed of the claimed invention (eg. the claimed invention constitutes new matter). In addition, the CAFC opined in Lockwood v. American Airlines Inc., 41 USPQ2d 1961 (Fed. Cir. 1977) that written description of an invention extends only to that which is disclosed in prior application, and does not extend to subject matter which is not disclosed, but would be obvious over what is expressly disclosed. The CAFC stated in Lockwood v. American Airlines Inc., 41 USPQ2d 1961 (Fed. Cir. 1977) that:

3. Patentability/Validity -- Specification -- Written description (§ 115.1103) Patent's entitlement to earlier filing date extends only to that which is disclosed in prior application, and does not extend to subject matter which is not disclosed, but would be obvious over what is expressly disclosed; one shows that one is "in possession" of invention of patent by

describing invention, with all its claimed limitations, not that which makes it obvious, and although prior application need not describe claimed subject matter in exactly same terms used in claims, prior specification must contain equivalent description of claimed subject matter, and description which renders obvious invention for which earlier filing date is sought is not sufficient.

The CAFC also stated in Lockwood v. American Airlines Inc., 41 USPQ2d 1961 (Fed. Cir. 1977) that:

The invention is, for purposes of the 'written description' inquiry, whatever is now claimed .") (emphasis in original). One does that by such descriptive means as words, structures, figures, diagrams, formulas, etc., that fully set forth the claimed invention. Although the exact terms need not be used in haec verba , see Eiselstein v. Frank , 52 F.3d 1035, 1038, 34 USPQ2d 1467, 1470 (Fed. Cir. 1995) (" [T]he prior application need not describe the claimed subject matter in exactly the same terms as used in the claims.. . . "), the specification must contain an equivalent description of the claimed subject matter. A description which renders obvious the invention for which an earlier filing date is sought is not sufficient.

7. No claim is allowed.

8. Papers related to this application may be submitted to Group 1600 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Papers should be faxed to Group 1600 at (703) 305-3014.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Ron Schwadron whose telephone number is (703) 308-4680. The examiner can normally be reached Monday through Thursday from 7:30 to 6:00. A message may be left on the examiners voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ms. Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Group 180 receptionist whose telephone number is (703) 308-0196.

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